

What is claimed is:

1. A method of treating cancer in a human, wherein the cancer expresses epidermal growth factor receptor (EGFR), comprising administering to the human a therapeutically effective amount of an antibody which binds ErbB2.
2. The method of claim 1 wherein the antibody blocks ligand activation of an ErbB receptor.
3. The method of claim 2 wherein the antibody blocks binding of monoclonal antibody 2C4 to ErbB2.
4. The method of claim 1 wherein the cancer is characterized by excessive activation of EGFR.
5. The method of claim 4 wherein the cancer overexpresses an ErbB ligand.
6. The method of claim 5 wherein the ErbB ligand is transforming growth factor alpha (TGF- α).
7. The method of claim 1 wherein the antibody blocks TGF- α activation of mitogen-activated protein kinase (MAPK).
8. The method of claim 1 wherein the cancer is not characterized by overexpression of ErbB2 receptor.
9. The method of claim 1 wherein the cancer is selected from the group consisting of colon, rectal and colorectal cancer.
10. The method of claim 9 further comprising administering a chemotherapeutic agent to the human.
11. The method of claim 10 wherein the chemotherapeutic agent is selected from the group consisting of 5-fluorouracil (5-FU), leucovorin (LV), CPT-11, and levamisole.
12. The method of claim 1 wherein the cancer is lung cancer.
13. The method of claim 12 wherein the cancer is non-small cell lung cancer.
14. The method of claim 12 further comprising administering a chemotherapeutic agent to the human.
15. The method of claim 14 wherein the chemotherapeutic agent is selected from the group consisting of a taxane, gemcitabine, navelbine, cisplatin, oxaplatin, and carboplatin.
16. The method of claim 1 wherein the antibody has a biological characteristic of monoclonal antibody 2C4.

17. The method of claim 16 wherein the antibody comprises monoclonal antibody 2C4 or humanized 2C4.
18. The method of claim 1 wherein the antibody is an antibody fragment.
19. The method of claim 18 wherein the antibody fragment is a Fab fragment.
20. The method of claim 1 wherein the antibody is not conjugated with a cytotoxic agent.
21. The method of claim 18 wherein the antibody fragment is not conjugated with a cytotoxic agent.
22. The method of claim 1 wherein the antibody is conjugated with a cytotoxic agent.
23. The method of claim 1 further comprising administering to the human a therapeutically effective amount of a second therapeutic agent selected from the group consisting of a second different antibody which binds ErbB2, a chemotherapeutic agent, an EGFR-targeted drug, an anti-angiogenic agent, an anti-hormonal compound, a cardioprotectant, and a cytokine.
24. The method of claim 1 comprising administering at least one dose of the antibody to the human in an amount from about 0.5mg/kg to about 10mg/kg.
25. The method of claim 24 comprising administering the dose about every week.
26. The method of claim 24 comprising administering the dose about every three weeks.
27. A method of treating cancer in a human wherein the cancer is not characterized by overexpression of the ErbB2 receptor, comprising administering to the human a therapeutically effective amount of an antibody which binds to ErbB2 and blocks ligand activation of an ErbB receptor.
28. The method of claim 27 wherein the cancer is breast cancer.
29. The method of claim 28 wherein the cancer is metastatic breast cancer.
30. The method of claim 28 further comprising administering a chemotherapeutic agent to the human.
31. The method of claim 30 wherein the chemotherapeutic agent is selected from the group consisting of an anthracycline antibiotic, cyclophosphamide, a taxane, navelbine, xeloda, mitomycin C, oxaliplatin, gemcitabine, and a platinum compound.
32. A method of treating cancer in a human comprising administering to the human therapeutically effective

amounts of (a) a first antibody which binds ErbB2 and inhibits growth of cancer cells which overexpress ErbB2; and (b) a second antibody which binds ErbB2 and blocks ligand activation of an ErbB receptor.

33. The method of claim 32 wherein the first antibody comprises monoclonal antibody 4D5 or humanized 4D5 and the second antibody comprises monoclonal antibody 2C4 or humanized 2C4.

34. A method of treating cancer in a human, wherein the cancer is selected from the group consisting of colon, rectal and colorectal cancer, comprising administering to the human a therapeutically effective amount of an antibody which binds ErbB2 and blocks ligand activation of an ErbB receptor.

35. An article of manufacture comprising a container and a composition contained therein, wherein the composition comprises an antibody which binds ErbB2, and further comprising a package insert indicating that the composition can be used to treat cancer which expresses epidermal growth factor receptor (EGFR).

36. An article of manufacture comprising a container and a composition contained therein, wherein the composition comprises an antibody which binds ErbB2 and blocks ligand activation of an ErbB receptor, and further comprising a package insert indicating that the composition can be used to treat cancer, wherein the cancer is not characterized by overexpression of the ErbB2 receptor.

37. An article of manufacture comprising (a) a first container with a composition contained therein, wherein the composition comprises a first antibody which binds ErbB2 and inhibits growth of cancer cells which overexpress ErbB2; and (b) a second container with a composition contained therein, wherein the composition comprises a second antibody which binds ErbB2 and blocks ligand activation of an ErbB receptor.

38. The article or manufacture of claim 37 further comprising a package insert indicating that the first and second antibody compositions can be used to treat cancer.

39. An article of manufacture comprising a container and a composition contained therein, wherein the composition comprises an antibody which binds ErbB2 and blocks ligand activation of an ErbB receptor, and further comprising a package insert indicating that the composition can be used to treat a cancer selected from the group consisting of colon, rectal and colorectal cancer.

40. A humanized antibody which binds ErbB2 and blocks ligand activation of an ErbB receptor.

41. The humanized antibody of claim 40 which binds ErbB2 essentially as effectively as murine monoclonal antibody 2C4.

42. The humanized antibody of claim 40 comprising a variable heavy (V_H) domain which comprises nonhuman

hypervariable region residues incorporated into a human V_H domain and further comprises a framework region (FR) substitution at a position selected from the group consisting of 69H, 71H and 73H, utilizing the numbering system set forth in Kabat (1991).

43. The humanized antibody of claim 42 comprising FR substitutions at positions 69H, 71H and 73H.
44. The humanized antibody of claim 40 comprising V_H domain complementarity determining region (CDR) residues GFTFTDYTMX (SEQ ID NO:7); DVNPNSGGSIYNQRFKG (SEQ ID NO:8); and NLGPSFYFDY (SEQ ID NO:9).
45. The humanized antibody of claim 40 comprising the V_H domain amino acid sequence in SEQ ID NO:4.
46. The humanized antibody of claim 40 comprising variable light (V_L) domain complementarity determining region (CDR) residues KASQDV SIGVA (SEQ ID NO:10); SASYXXX (SEQ ID NO:11); and QQYYIYPYT (SEQ ID NO:12).
47. The humanized antibody of claim 40 comprising the V_L domain amino acid sequence in SEQ ID NO:3.
48. The humanized antibody of claim 40 which is an intact IgG1 antibody.
49. The humanized antibody of claim 40 which is an antibody fragment.
50. The humanized antibody of claim 49 which is a Fab fragment.
51. An affinity matured antibody which binds ErbB2 and blocks ligand activation of an ErbB receptor.
52. A composition comprising the humanized antibody of claim 40 and a pharmaceutically acceptable carrier.
53. An immunoconjugate comprising the humanized antibody of claim 40 conjugated with a cytotoxic agent.
54. Isolated nucleic acid encoding the humanized antibody of claim 40.
55. A vector comprising the nucleic acid of claim 54.
56. A host cell comprising the vector of claim 55.
57. A process of producing a humanized antibody comprising culturing the host cell of claim 56 so that the nucleic acid is expressed.

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1. *Staphylococcus aureus* (1000)
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